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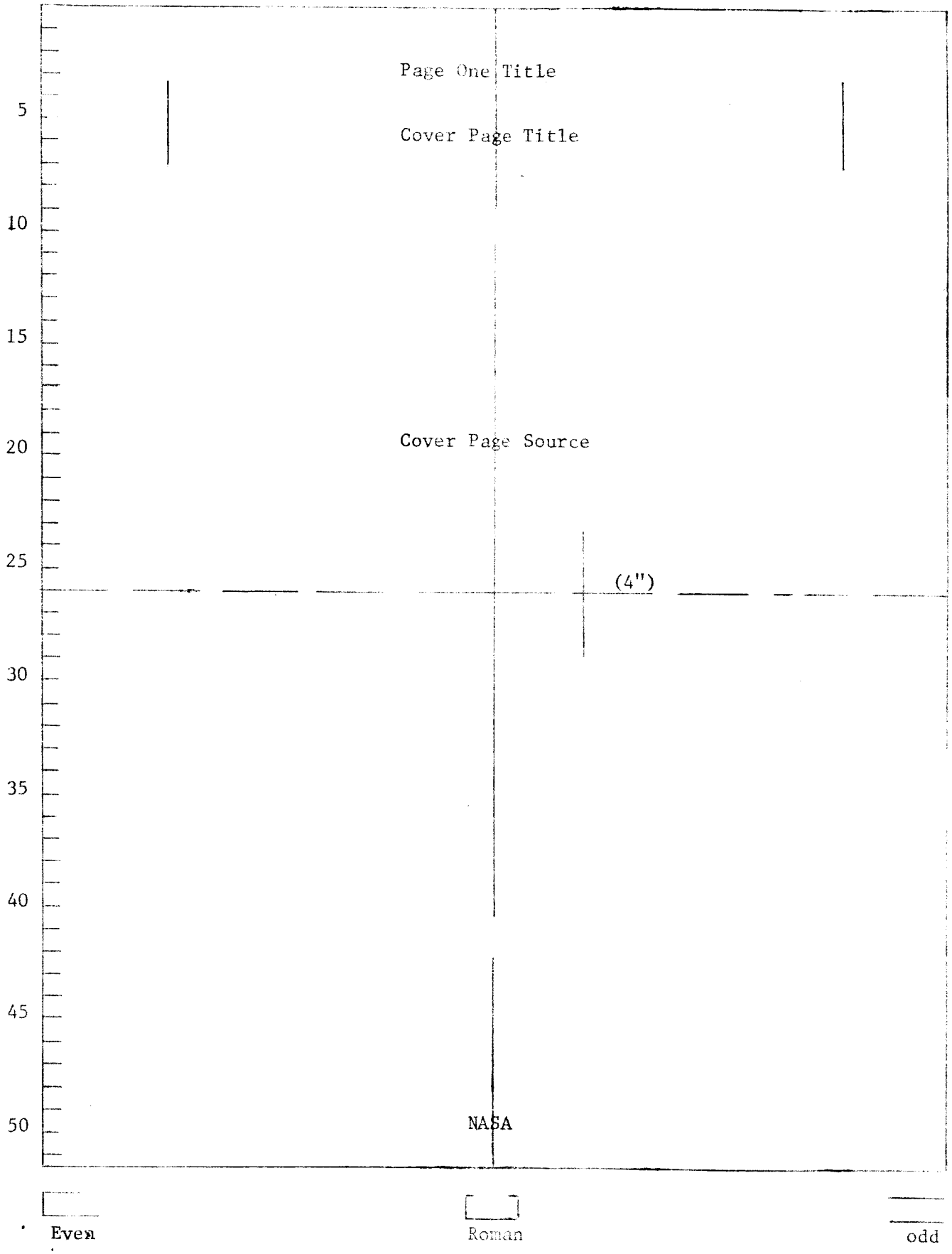
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INFLUENCE OF EAST-WEST AND RETURN TRIPS ON THE CIRCADIAN RHYTHMS OF DIURESIS AND URINARY ELIMINATION OF SODIUM AND POTASSIUM*

E. LaFontaine, J. Sirot, J. Pasquet and J. LaVernhe
Medical Service of Air France, 1 Square Max Hymans, Paris 15

ABSTRACT. Diuresis and urinary elimination of sodium and potassium were measured for a group of 10 subjects by collecting 24-hour urine samples in six 4-hour segments, which allowed us to establish circadian oscillations of the eliminations (2/24 hour percentage in each specimen). Eight and two subjects were used in varying stopover and flight periods in Paris and Anchorage.

The biological rhythms of any periodicity (annual, monthly, daily) and /11** in all species, whether vegetable or animal, have been and continue being the object of numerous studies. Among many others, the works by Bunning [3] and Reinberg and Ghata [11] constitute excellent exponents of current knowledge based on considerable bibliographic data. The studies performed by Halbert [5] are among the best known in the field of experimental medicine. In France, Raboutet et al. [10] made a study of the circadian perturbations resulting from long-distance flights. Benitte and LeFevre-Desnouettes [2], based on theory, suggested directing research toward the inversion of the nychthemeral rhythms of the flight crew member as he passes through 12 time zones. Strughold [13], Aschoff [1], Gerritzen [4], Hauty and particularly Adams [6] performed tests during long distance east-west and return flights. Finally, Schreuder [12] compiled a certain number of bibliographic elements concerning the role played by circadian perturbations in commercial jet pilot fatigue.

In a preliminary investigation [8 and 9] our Medical Service analyzed the comments of 312 crew members flying the North Atlantic routes. More than two thirds of the subjects complained about troubles which they attribute to schedule shifts: essentially troubles with sleep, but also digestive troubles. After a trip encompassing six time zones, about one third of the subjects declared that they sleep normally starting with the first night, one third starting with the second night and one third finally after three nights or more. Upon their return to Paris the difficulties of readapting to local time appeared the more pronounced, the longer they stayed on the American continent.

Following this investigation, based on purely subjective impressions, we tried to collect objective data by establishing before, during and after the flights, the circadian variations of a certain number of biological parameters in a group of ten subjects.

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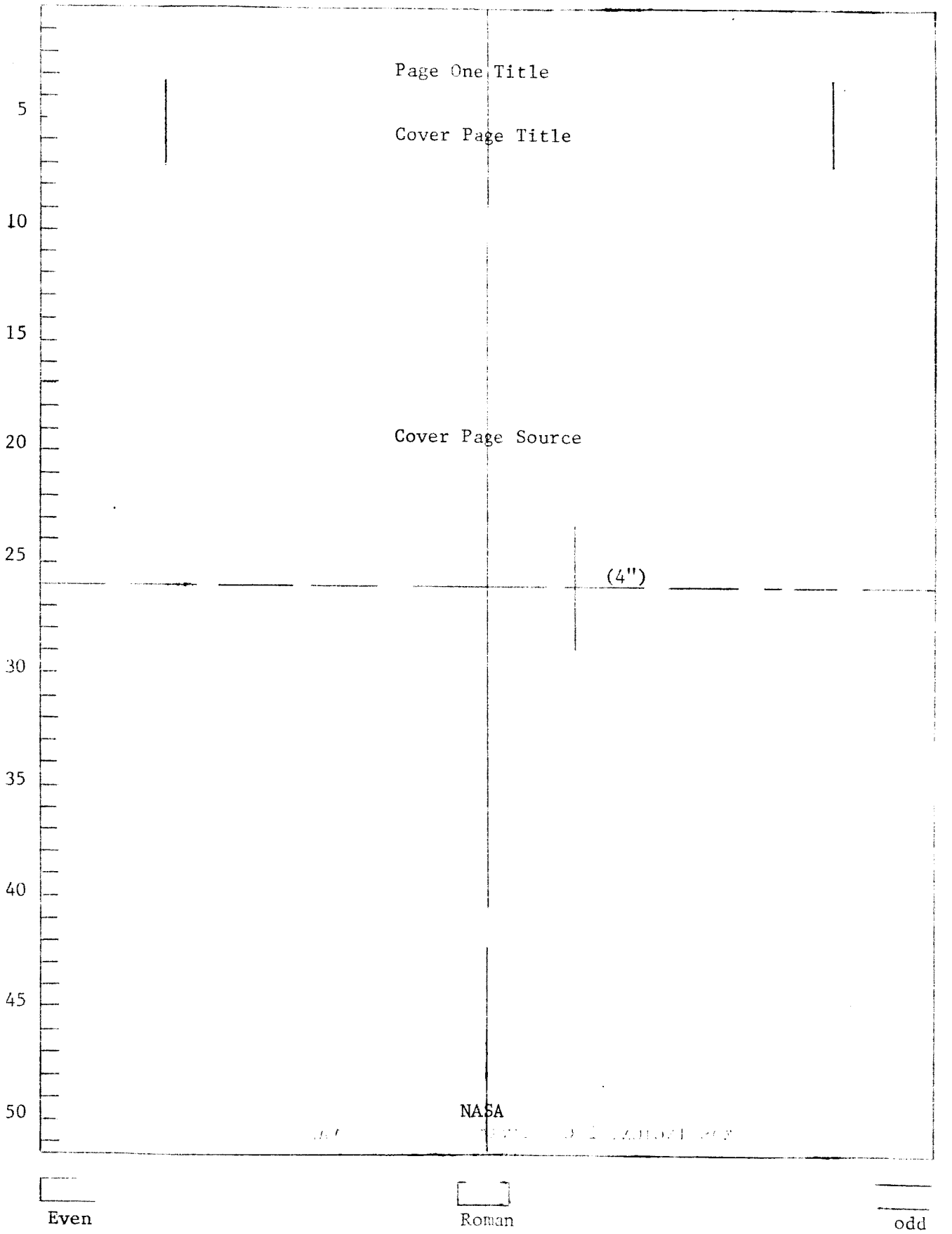
*Study Made with the Technical Cooperation of J. Ghata.
**Numbers in the margin indicate pagination in the foreign text.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Since suprarenal activity and hydroelectrolytic control of the organism is closely conditioned by the nychthemeral and since each of their variations is immediately reflected in urinary excretions, the following parameters were obtained initially:

1. Diuresis, urine sodium and potassium for hydroelectrolytic equilibrium.

2. 17 ketosteroids and 17 OH corticosteroids in the urine for cortico-suprarenal activity.

3. 4-hydroxy-3-methoxy-mandelic acid and urinary norepinephrine for medullo-suprarenal activity.

The results of these tests were published elsewhere [7]. The purpose of this work is to analyze the figures obtained by diuresis, natriuria and kaliuria.

Diuresis was determined to be almost 10 ml, sodium and potassium were determined by flame photometry. The nychthemeral variations of the eliminations were established by collecting all the urine for 24 hours in six separate specimens of equal duration, i.e. 4 hours.

Establishment of Circadian Test Sample Variations /12

A first experimental phase consisted of establishing the circadian test sample curves of the subjects selected in Paris. Determinations were made from each of six 4-hour specimens collected daily for a period of 7 consecutive days among eight subjects subjected to a similar diet regimen.

For each parameter, the average and the standard deviation for 8 subjects and for the 7 days were calculated in each of the 6 daily urine specimens. Since the absolute value of the 4-hour and 24-hour excretions were subject to many factors of variation beyond the nychthemeral oscillations, we related the 4-hr fractionated eliminations to the total 24 hour excretion by establishing the 4/24-hour percentage in each specimen.

Table 1 is a graphic representation of the results so obtained. Each curve is accompanied by its standard deviation. The three circadian variations are by and large coincident. For the diuresis, the sodium and the potassium content, a maximum daytime elimination peak in the urine samples was found from 2-6 p.m. In contrast, a minimum nocturnal constant is detected in the urine specimens from 2 to 6 a.m. The most pronounced variation and the lowest standard deviations apply to potassium; urine elimination of this ion thus appears to be particularly interesting for the study of the biological circadian rhythms.

Experimental Flight Conditions

The Paris-Anchorage route, covered in a Boeing 707 was selected, since a polar route is involved, thus a North-South axis, in view of the major schedule

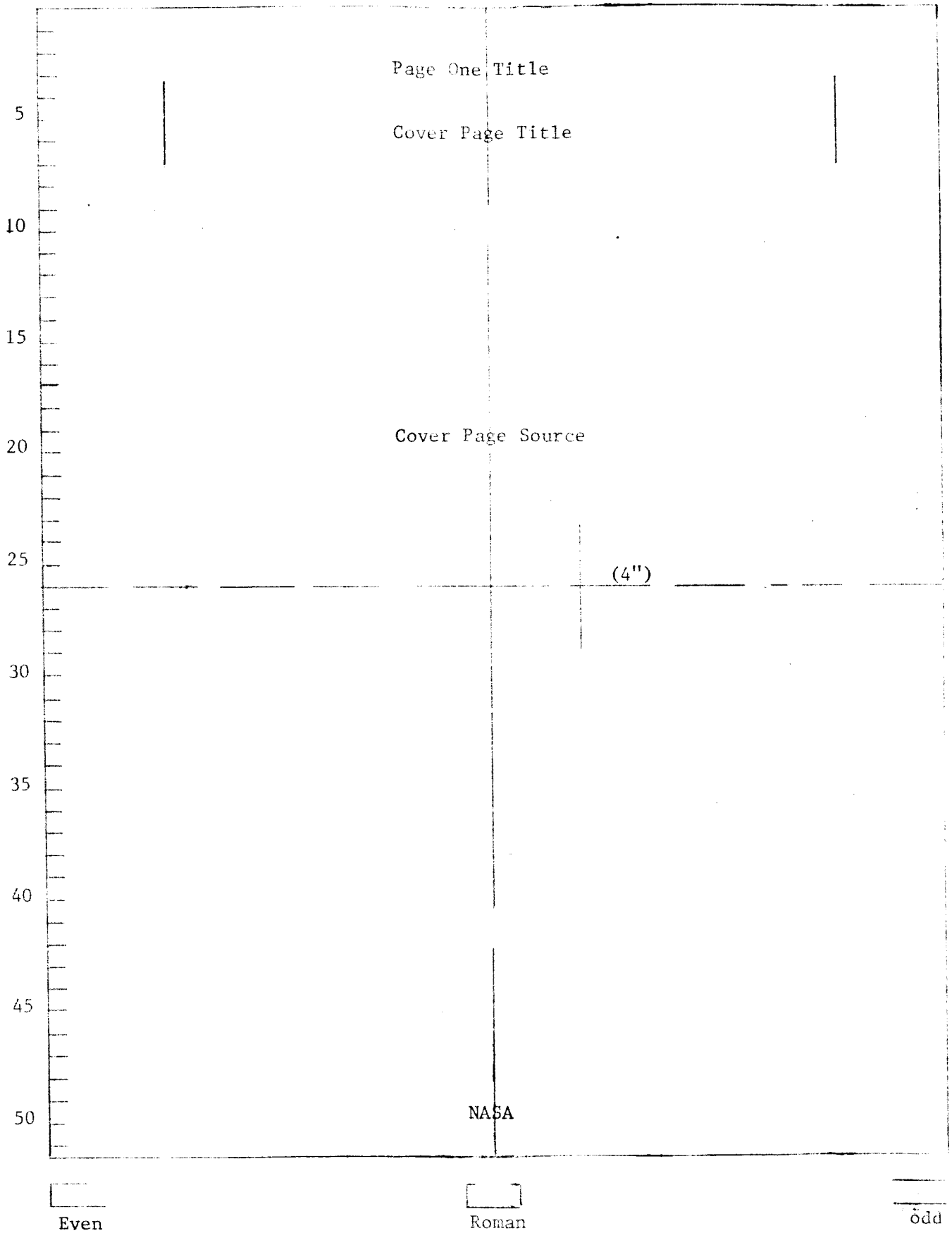
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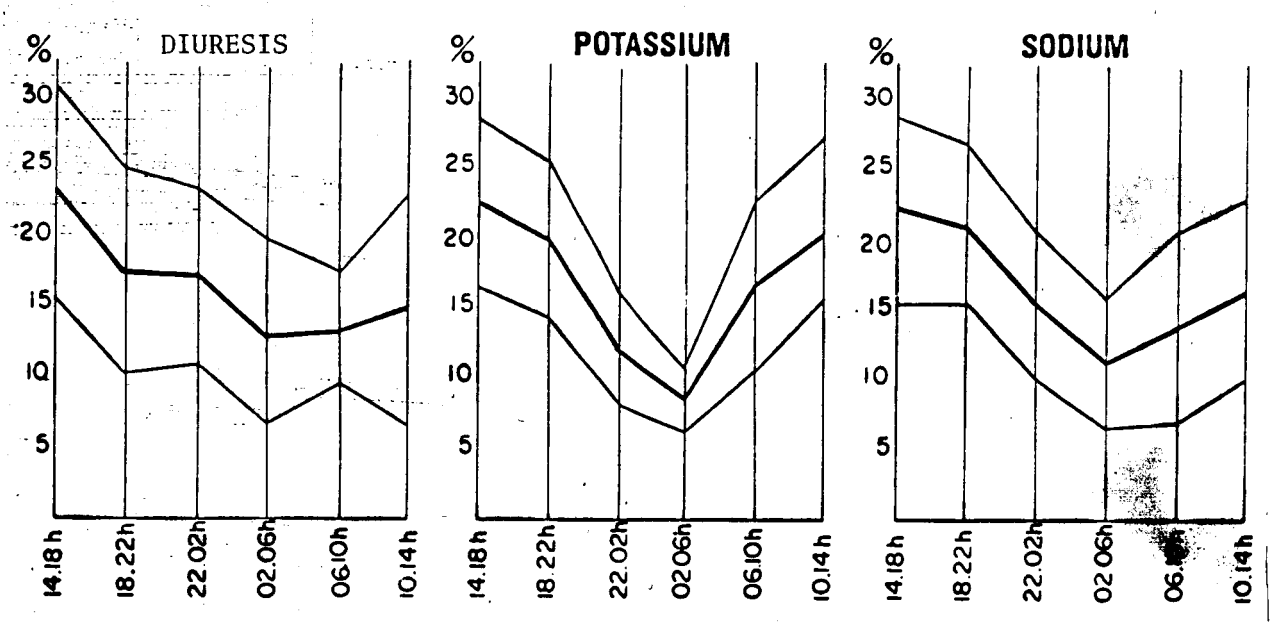
TABLE 1. SAMPLE CIRCADIAN VARIATIONS OF URINE ELIMINATIONS, EXPRESSED AS A PERCENTAGE OF 24-HOUR ELIMINATION

Average of 8 subjects for 7 reference days. The standard deviation is shown on each side of the curve.

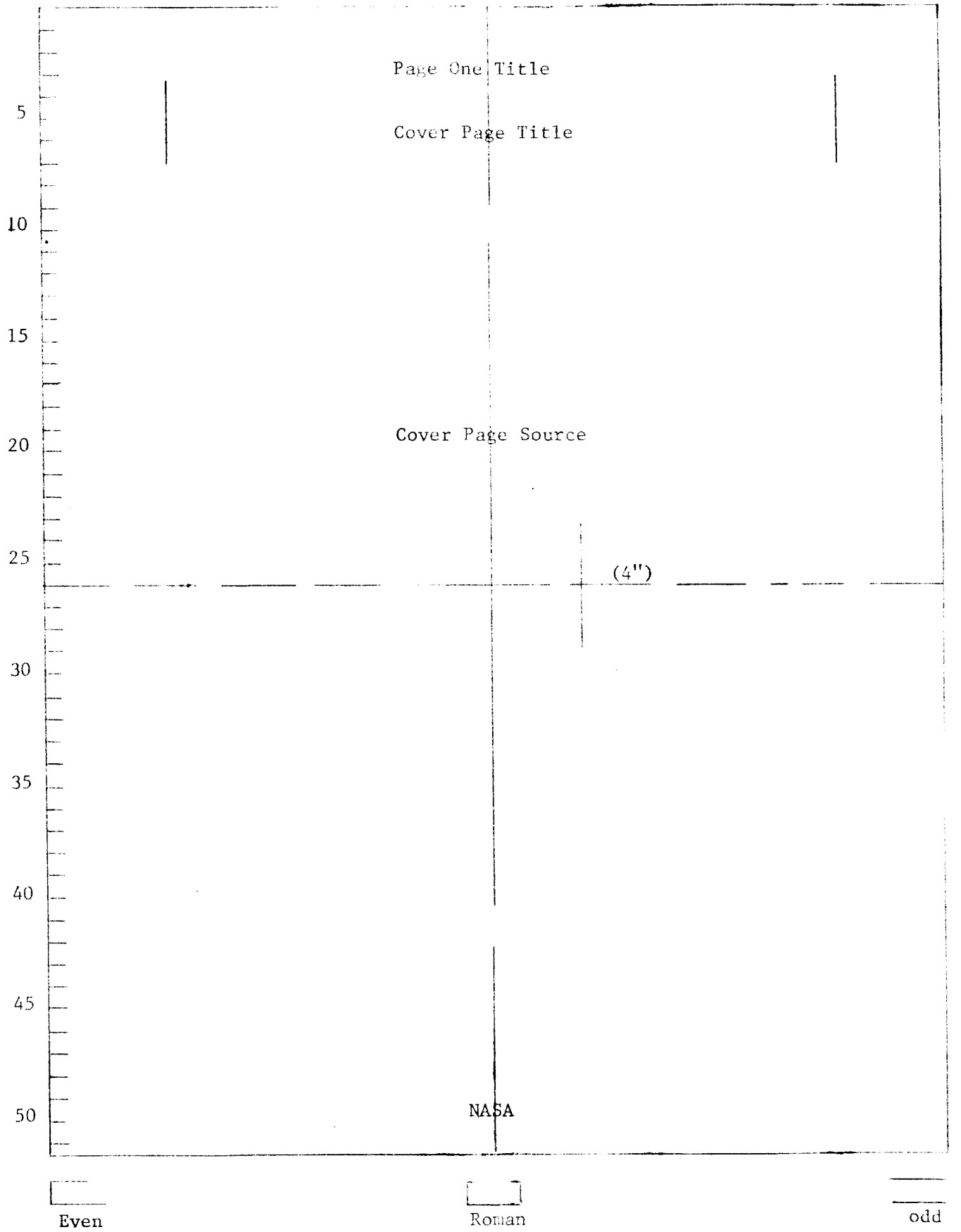


deviation (11 hours) which separates the two cities and in view of the rapidity of this shift (approximately 11 hours of flight).

All the tests followed the schedule described below: /13

OUTBOUND			RETURN		
	Paris Time	Anchorage Time		Paris Time	Anchorage Time
Paris Anchorage	2:45 p.m. 2:15 a.m.	3:45 a.m. 3:15 p.m.	Anchorage Paris	10:00 p.m. 9:05 a.m.	11:00 a.m. 10:05 p.m.

It can be seen that if one observes local Anchorage time upon arrival, having to sleep from 10 p.m. to 7 a.m., this is equivalent, in French time, to a rest period between 9 a.m. and 6 p.m. after a workday of 24 + 11 hours = 35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hours. Conversely, upon his return, the workday is shortened during the flight and is no more than 24 - 11 = 13 hours. If the individual is previously accustomed to Alaska time, he arrives in Paris at 9 a.m., i.e. in fact, at 10 p.m. biological time: it is time to lie down when the workday begins. These experimental conditions are therefore excellent, since they correspond to an almost total inversion of the nychthemeral.

Experimental Results During a Fast Paris-Anchorage-Paris Round Trip

After arriving in Alaska at 3:15 p.m. (local time), a test group of 8 physicians aged 38 to 48, already tested in Paris during the 7 preceding days, departed the following morning at 11 a.m. (local time), maintaining the same regimen as the crew throughout the trip. This 20-hour stopover includes a nocturnal rest period which actually is a daytime rest period if referenced to French time.

The curves are always expressed in a 4:24-hour percentage ratio. The experimental curves of the diuresis, the natriuria, and the kaliuria (an average of 8 subjects) during the trip were superimposed upon the pre-established test control curves (Table 2). The experimental standard deviations published elsewhere with the absolute values of the excretions [7] are similar /14
to the standard deviations contained in Table 1 for the control curves.

The flight periods entailed a reduction of the diuresis and eliminations considered and are followed by an excretion "rebound" following the flight. During the return trip to Paris, the experimental variations immediately returned in accordance with the circadian control curves which is a sign of the absence of any effect caused by the shift in schedule on the biological activities under investigation.

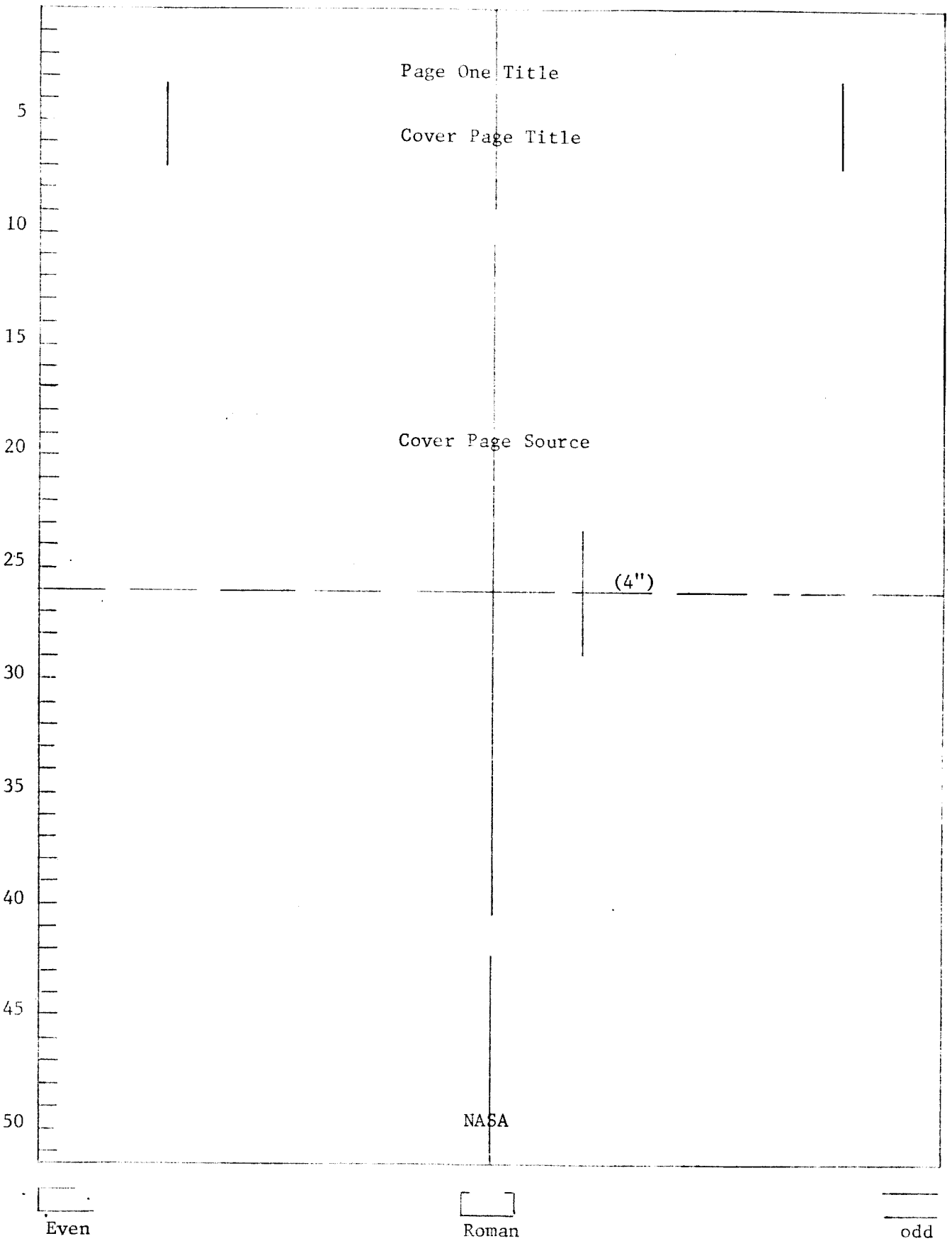
Experimental Results During a Round-Trip Paris-Anchorage-Paris Flight With a Five-Day Stopover in Anchorage

The trip went as follows:

1. First day: Paris-Anchorage flight.
2. Five-day stopover in Anchorage.
3. Seventh day: Anchorage-Paris flight.

Instead of investigating an average by studying a group of subjects, in this case a longitudinal individual study of only two subjects is involved. The control excretion rhythms of each of these two subjects, instead of a 7-day period, were established for 22 consecutive days preceding the departure. The experimental determinations were started on the take-off day and continued every 4 hours throughout the stopover in Alaska and during the return flight until the arrival in Paris.

Table 3 shows the experimental curves of the diuresis, the sodium and potassium eliminations superimposed on the pre-established control curves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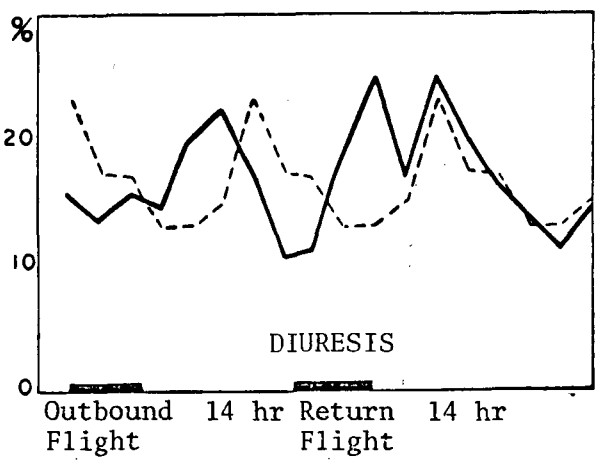
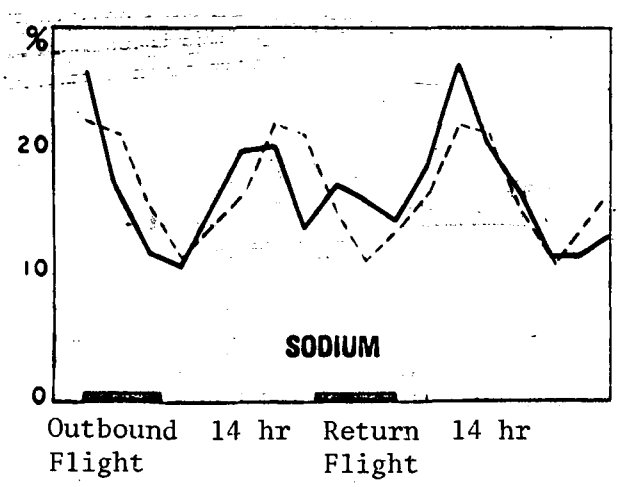
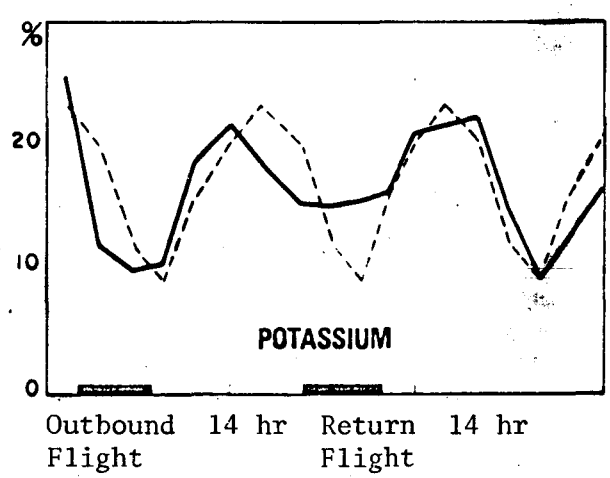
(4:24 hour ratio) for one of the subjects. The detailed numerical values and standard deviations were contained in a publication quoted earlier [7].

TABLE 2. EXPERIMENTAL CIRCADIAN VARIATIONS OF URINARY ELIMINATIONS (Solid Line) COMPARED TO CONTROL VARIATIONS (Broken Line)

Average of 8 Subjects During a Quick Paris-Anchorage-Paris Round Trip
Figures Expressed in 4:24-Hour Percentage Ratios







The trip to Anchorage entailed a clear modification of the circadian variation in the form of a progressive retardation of the maximum and minimum points. This modification begins on the third day after the arrival in Alaska with a 4-hour retardation with respect to the control curve. It becomes most pronounced on the fifth day for potassium with a shift of two or even three periods of 4 hours each affecting then the excretions studied and resulting in a complete inversion with respect to the criteria established before the flight. /15

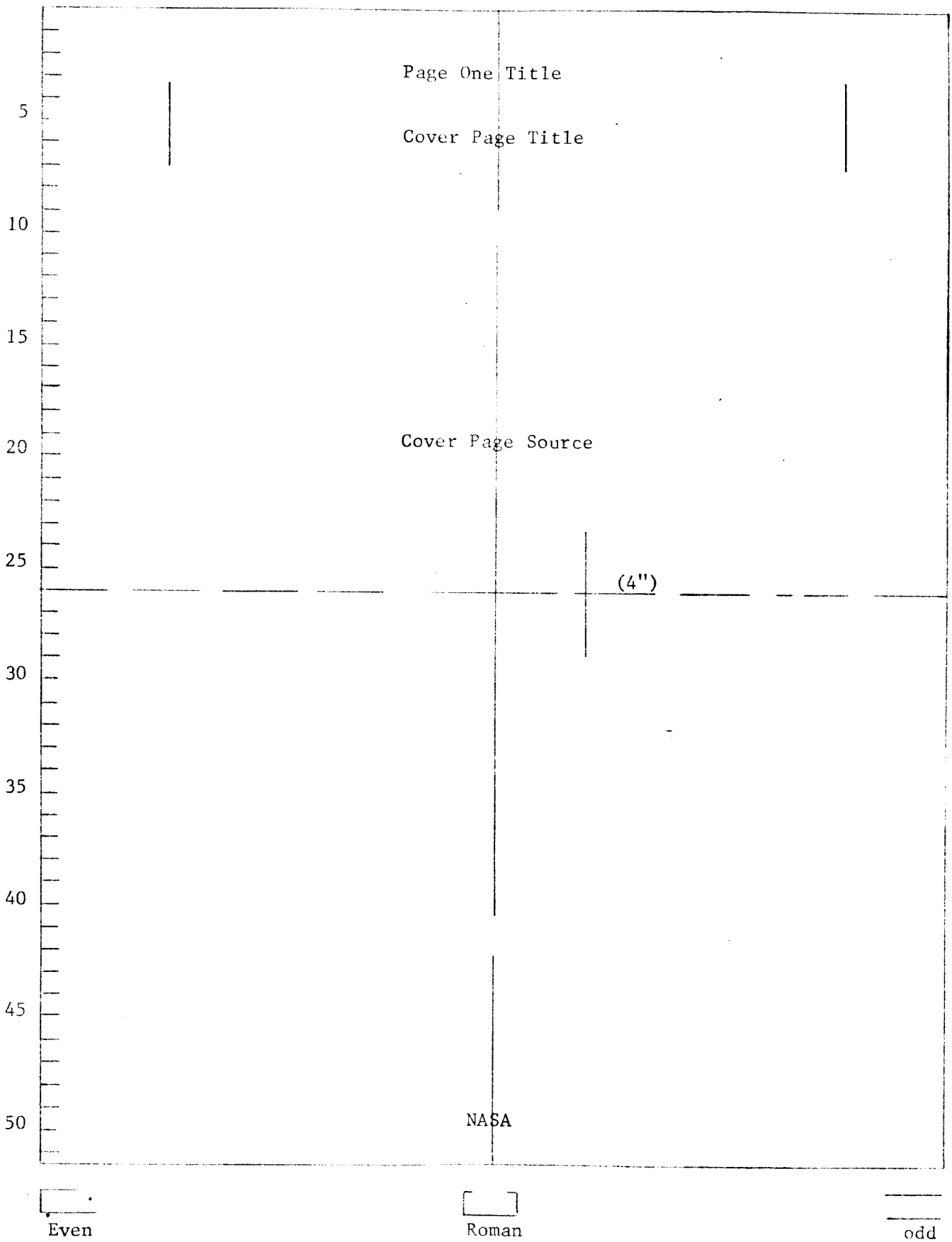

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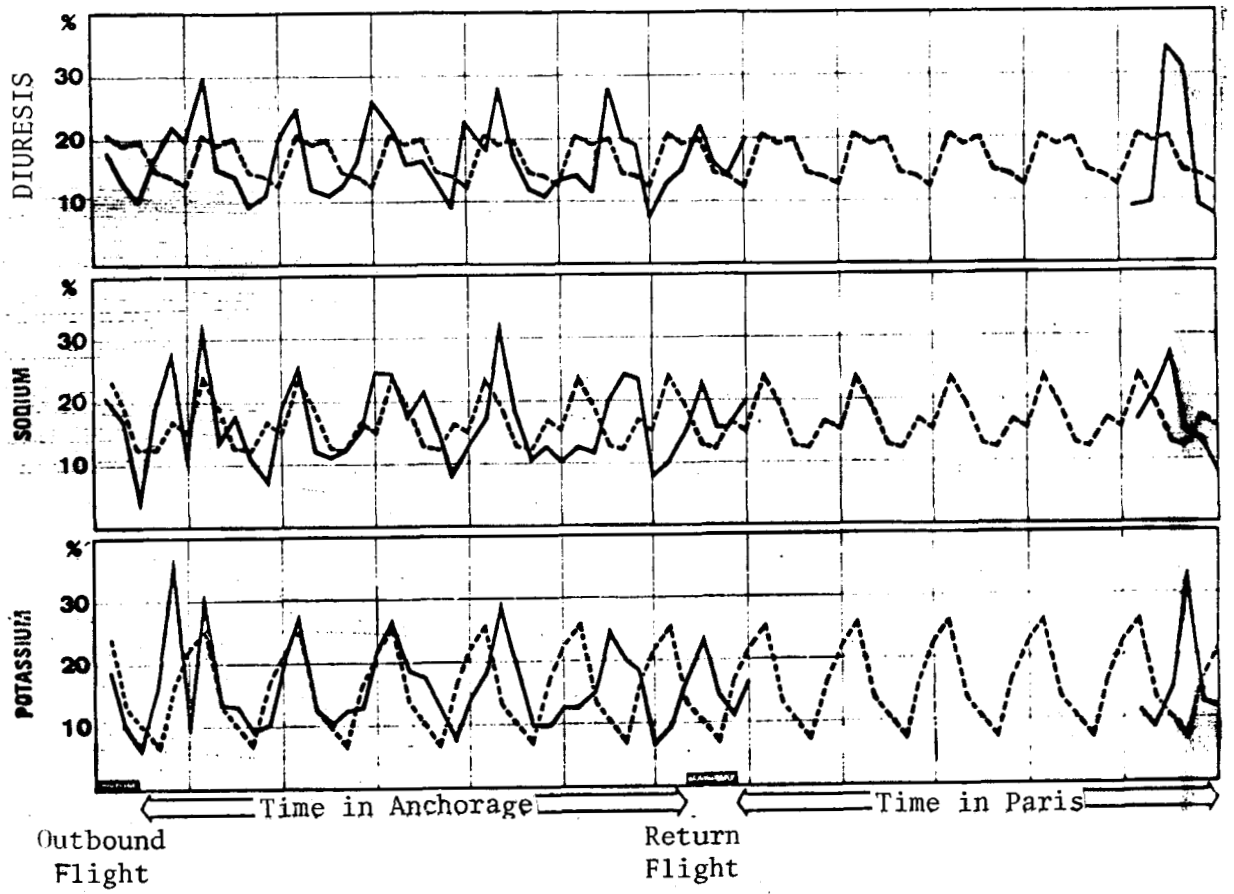
TABLE 3. EXPERIMENTAL CIRCADIAN VARIATIONS OF DIURESIS, URINARY SODIUM AND POTASSIUM (Solid Line) COMPARED WITH CONTROL VARIATIONS (Broken Line) EXPRESSED IN 24-HOUR ELIMINATION PERCENTAGE VALUES

Results of One Subject During a Paris-Anchorage-Paris Flight With a 5-Day Stopover in Anchorage

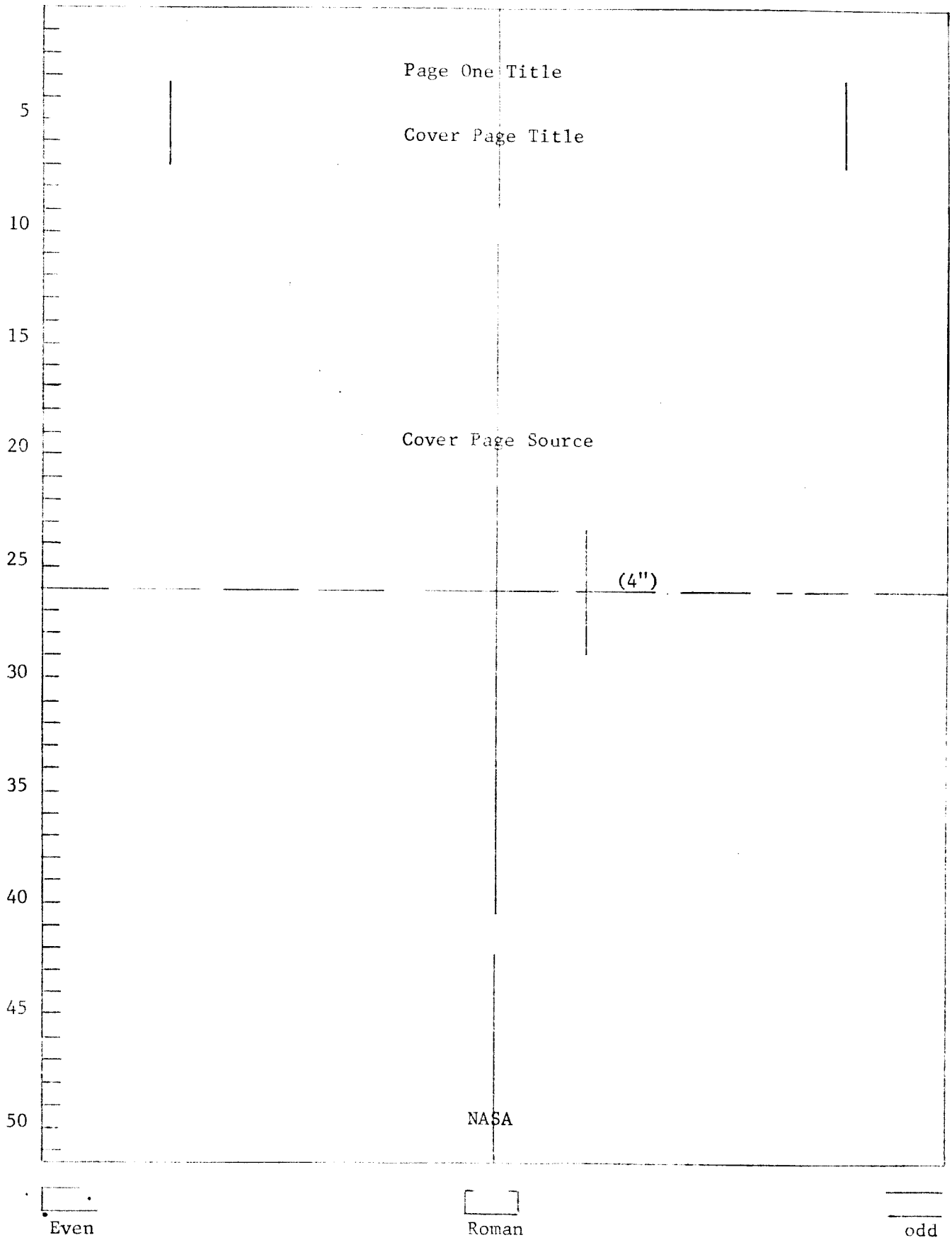
The Vertical Lines Stand for 24-Hour Periods, Calculated From 2 p.m. to 2 p.m.



After the return trip, these modifications continued and on the fifth day the circadian variation preceding the experiment is not found again. However, these experiments require a more accurate study for control purposes and need to be extended into the time period following the return to Paris so as to better assess the readaptation time to the French time.

Conclusions

This experiment led to the following conclusions: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1. A flight phase of about 11 hours is accompanied by a significant reduction of diuresis, natriuria and kaliuria during the flight and a "rebound" phenomenon with hypersecretion occurs after the flight.

2. After a rapid round trip with a 20-hour exposure to a negative time shift of 11 hours, the circadian water elimination rhythm of sodium and potassium immediately returns together with the pre-existing control rhythm.

3. During a trip involving a 5-day exposure to a negative 11-hour time shift, the circadian elimination rhythm of the same elements begins to adapt to the local time on the third day. This adaptation is complete on the fifth day while the excretion rhythms are then in opposition with the pre-established control rhythms.

4. Urinary potassium which presented a clear-cut circadian variation and a relatively minor standard deviation among the average subjects tested, appeared of particular interest in the study of hydroelectrolytic circadian modifications of the organism.

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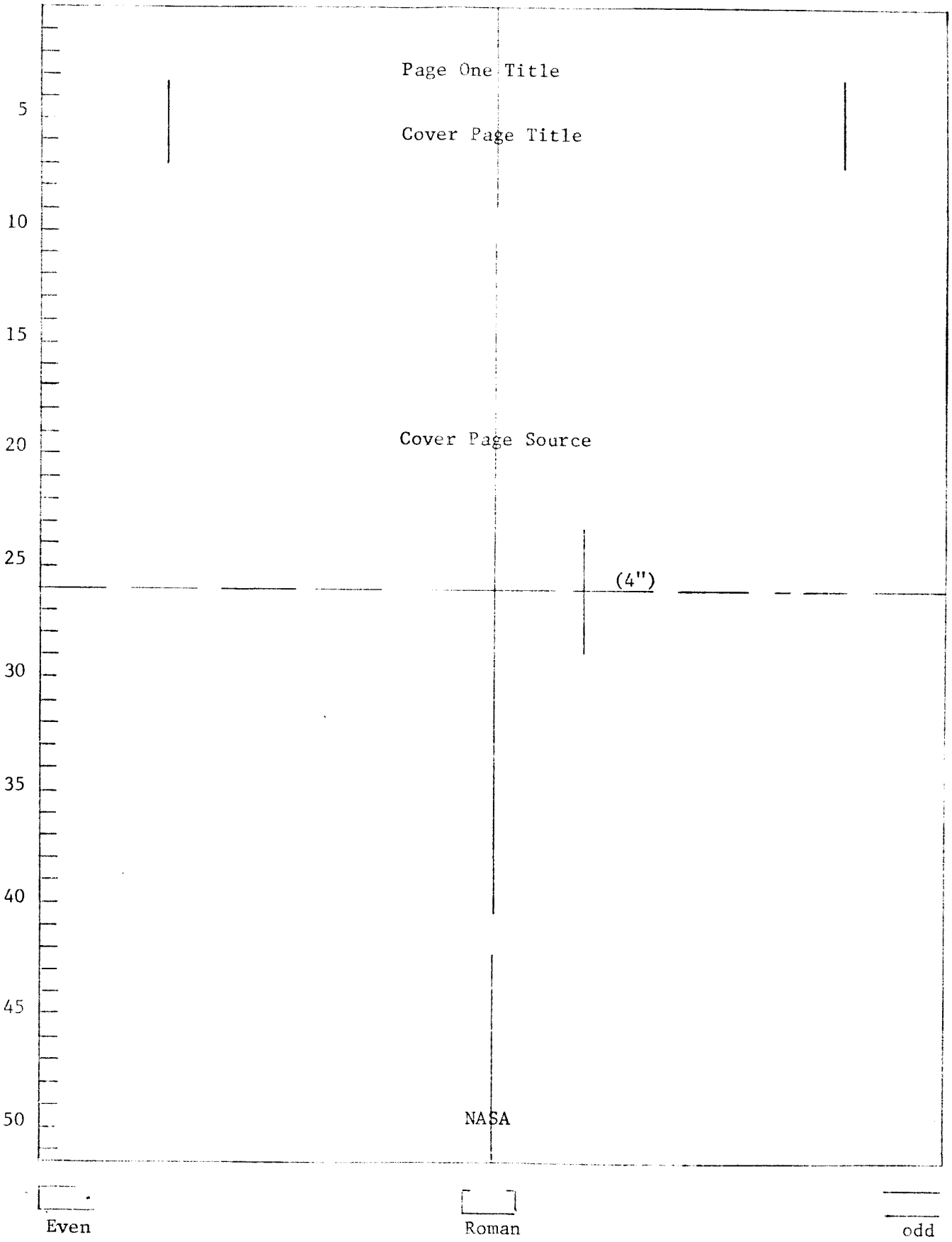
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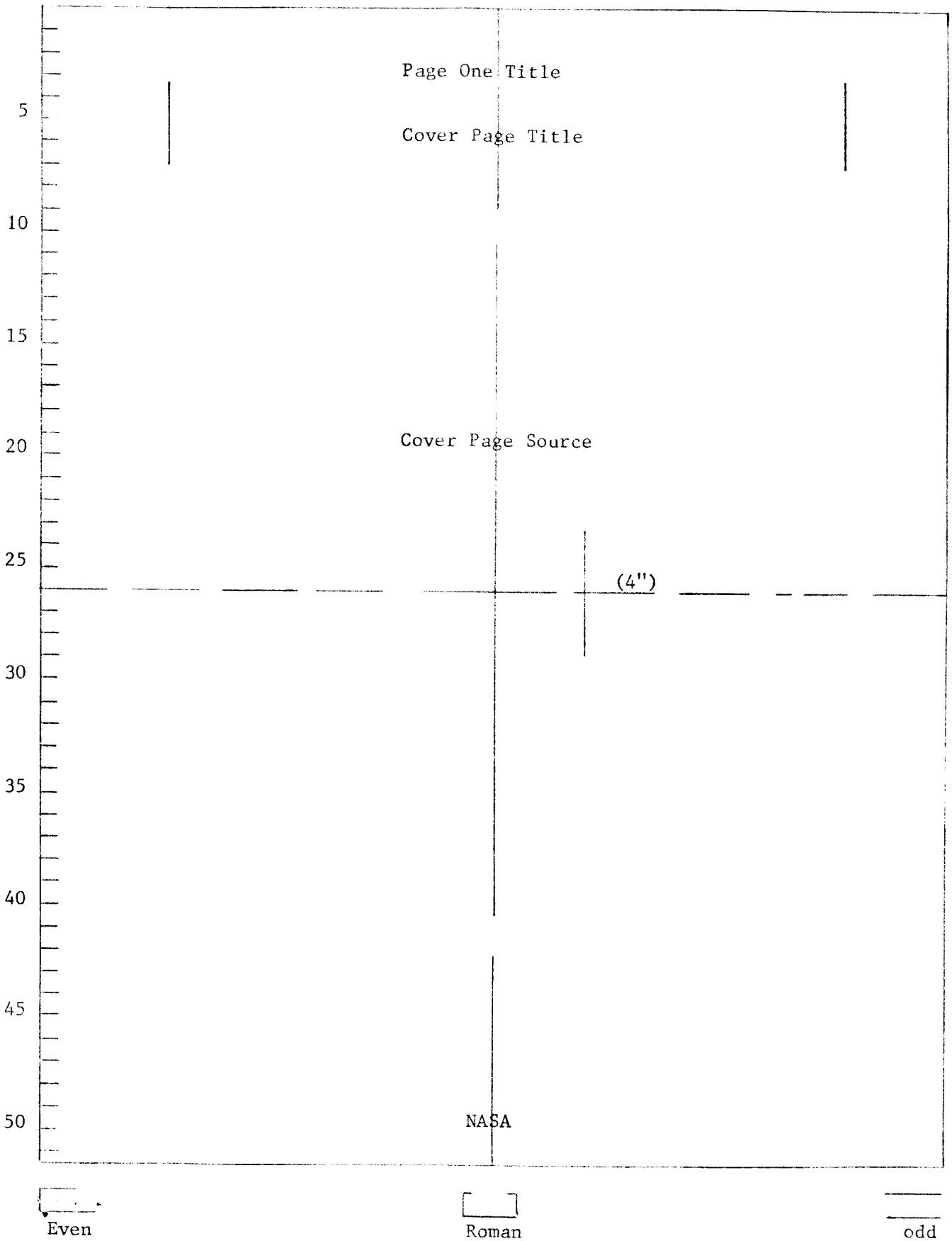
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